

AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGAC  
 CACGCCGACAGAAAACCTACTAAGGCCATCTCAGGGGTGCCTGTGCCAGGAGA  
 GGGGGGCGGTGTCCCCGGGCGCAGAGCCATGCCTTTCGGCCTGAAGCTCCG  
 CAGGACTCGGCGCTACAACGTCCTGAGCAAGAACTGCTTTGTTGCCCGGATC  
 CGCCTGCTGGACAGCAATGTCATCGAGTGCACGCTGTCGGTGGAAAGCACGG  
 GGCAAGAGTGCCTGGAGGCCGTGGCCCAGAGGCTGGAGCTGAGGGAGACGC  
 ACTACTTCGGCCTTTGGTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGTTAGA  
 GCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTG  
 CTTTTCTTCGGAGTCATGTTCTATGTGCCAAATGTGTACACGGCTTCAGCAGGA  
 GGCCACAAGATATCAGTATTACCTGCAAGTCAAAAAGACGTGCTTGAAGGA  
 CGGTTGCGGTGCTCCCTGGAACAAGTGATCCGGCTGGCTGGCTTAGCTGTGC  
 AAGCTGACTTCGGAGATTATAACCAAGTTTGATTCCCAAGAGTTCCTCCGAGA  
 GTATGTGCTCTTTCCTATGGATTTGGCCATGGAGGAGGCGGCTCTGGAGGAG  
 CTAACCCAGAAGGTGGCCCAGGAACACAAAGCTCATAGCGGGATCCTGCCG  
 GCTGAAGCTGAAGTGTACATCAACGAGGTAGAGCGTTTGGATGGATTTG  
 GACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGACCTCGG  
 CATCTTCTTCATGGGGATTTTGTGAGGAACAGGGTCGGGAGACAGGCAGTG  
 ATATACAGGTGGAATGACATTGGGAGTGTTACTCACAGCAAAGCAGCCATCC  
 TGTTGGAGCTGATTGACAAGGAGGAGACCGCGCTCTTCCATACAGATGATAT  
 TGAAAATGCCAAGTACATTTCTCGGTTGTTTACCACTCGGCACAAATTTTACA  
 AACAGAACAAGATCTGCACTGAACAGTCAAATTCTCCACCCCCAATCAGACG  
 CCAGCCCACCTGGAGCCGGTCCCTACTGCCAAGGCAGCAGCCGTATATCTTG  
 CCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCATACTTCCCA  
 AGACAGCATTTTCCCCGGGAACGAAGAAGCCTTGTACTGCCGTTCTCACAAAC  
 AGCCTGGACCTTAATTACTTGAACGGCACCGTCACCAATGGCAGCGTGTGCA  
 GCGTTCACAGCGTCAACTCCCTCAGCTGCTCCCAGAGCTTCATTCAGGCGTCT  
 CCAGTGTCTCCAACCTTAGCATCCCTGGGAGTGACATCATGAGGGCCGATT  
 ACATCCCCAGCCACCGCCACAGCACCATCATCGTGCCGTCTTACAGGCCGAC  
 CCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCTGATGCACGC  
 AGACAGCCAGAGCCGGTCTCTGCGTAACTCAATATCATCAACACCCATGCC  
 TATAACCAGCCCGAGGAAGTGGTGTACAGCCAGCCGGAGATGCGGGAGAGG  
 CATCCCTACACGGTCCCCTATGCACACCAGGGGTGCTACGGTCACAACTTG  
 TAAGTCCGTCTGACCAGATGAACCCCCAAAATTGTGCGATGCCTATCAAGCC  
 AGGGGCCAGTTCATCTCTCACACAGTGAGCACTCCAGAACTAGCCAACATG  
 CAGCTCCAAGGAGCACAACTATAGCACAGCCCACATGCTCAAGAACTATC  
 TATTCAGGCCGCCACCCCTTACCCTCGGCCCGTCCTGCCACCAGCACCCCA  
 GACCTCGCCAGCCACCGCCACAAGTACGTCAGCGGCAGCAGCCCTGATCTGG  
 TAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACC  
 TGTGGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCTCACAGCCACCAAG  
 CACCATGGCGGCGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTG

FIGURE 1A

ATGAACAGCATGGTGAGAGGCATGGAGGCCATGACACTGAAGTCACTCAATA  
 TCCCCATGGCTCGCCGCAACACCCTTCGGGAGCAGGGCCCTTCCGAGGAGAC  
 GGGCGGCCACGAAGTGCACGGTCTCCCCCAGTATCACCACAAGAAGACATTC  
 TCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGAGGAGGAG  
 ACCCTGGAGGCTGCACCTCAGGTTCTGTGCTTCGAGAGAAAGTAGAATACA  
 GTGCCCAGCTGCAGGCTGCCCTGGCCCCGCATCCCCAACAGGCCCCCACCTGA  
 GTACCCAGGGCCAAGAAAAAGTGTGAGTAATGGGGCACTGAGACAGGACCA  
 GGGAACCCCTCTTCTGCCATGGCCAGGTGCAGGGTGCTGAGACACGGACCA  
 TCCAAGGCCCTCAGTGTCTCCCGGGCAGAGCAGCTGGCTGTCAACGGTGCCT  
 CTCTGGGTCCCTCCATCTCTGAGCCTGACCTAACCAGCGTGAAGGAGCGGGT  
 CAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGTGAGAGATGTTCTCCCTGGAG  
 GACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAAG  
 ATGACGGGCCCCGCAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAAT  
 GGGCTCTCGGTGGCCCGAGTGTGCGGGGCGGGAAGATGGTCGCCATGATGCCA  
 CCCGAGTCCCCATAGACGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAG  
 ATGGAATGGTGTTCACAGAATATGAGCAGATTCCAAACAAAAAGGCCAACG  
 GCGTCTTCAGCACCGCCACTCTGCCTGAGAACGCCGAGCGCAGCCGGATCCG  
 AGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCCGACCAAAGAA  
 AACAAACACAGGCTATATCAACGCCTCCCACATCAAGGTGGTGGTCCGGCGGAT  
 CAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGA  
 CTTCTGGCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACT  
 GCAGAGGAGGAGGGTGGACGGACCAAAAGCCATCGATACTGGCCCCAACTG  
 GGGTCCAAGCATAGTTCTGCCACCTACGGCAAGTTCAAGGTCACCACAAAGT  
 TCCGGACAGATTCTGGTTGCTATGCAACGACGGGCCCTAAAGGTGAAGCACCT  
 GCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGACGTACACGGACTGGCCC  
 CACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTGTCTACTTGGAGGAAA  
 TCCAGTCAGTCCGACGCCACACCAACAGCGTGCTGGAAGGCATCAGGACCAG  
 GCACCCCCCATCGTGGTTCCTGACGCGCGGGTGTGGGAAGGACTGGTGTG  
 GTTATCCTCTCTGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGG  
 AGGTGCCCACGATGCTGCGATTCTCAGGGAGCAGAGGATGTTTCATGATCCA  
 GACCATTGCGCAGTACAAGTTCGTCTACCAAGTCCTCGTCCAGTTCCTGCAGA  
 ATTCCAGGCTCATTTGATCTCCTCCGGGATGCAGCTTCTGGAGGAGGGACGC  
 AGCTCTGTCTGACAGGGGGCGGCCACTTCGACAACATCTGCCTCCCCCAGCC  
 AGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATCA  
 TGTATTATTTTATATAAGATAATTTATTTTTTCCCTCTTTGGAATAAGTTCTG  
 TGAGTTATTATATAATGCTTCCCCCCCCATACACACACAATAATATAGTGCT  
 TCTCATTTG (SEQ ID NO:1)

FIGURE 1B

underlined = deleted in targeting construct

**bold** = sequence flanking Neo insert in targeting construct

AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGACCACGCCGA  
 CAGAAACTACTAAGGCCATCTCAGGGGTGCCTGTGCCAGGAGAGGGGGGCGGTGTCCCC  
 GGGCCGCAGAGCCATGCCTTTCGGCCTGAAGCTCCGCAGGACTCGGCGCTACAACGTCTT  
**GAGCAAGAACTGCTTTGTTGCCCGGATCCGCCTGCTGGACAGCAATGTCATCGAGTGCAC**  
**GCTGTCCGTGGAAAGCACGGGGCAAGAGTGCCTGGAGGCCGTGGCCCAGAGGCTGGAGCT**  
**GAGGGAGACGC**ACTACTTTCGGCCTTTGGTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGT  
 AGAGCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTGCTTTT  
 CTTCCGAGTCATGTTCTATGTGCCAAATGTGTCACGGCTTCAGCAGGAGGCCACAAGATA  
 TCAGTATTACCTGCAAGTCAAAAAAGACGTGCTTGAAGGACGGTTGCGGTGCTCCCTGGA  
 ACAAGTGATCCGGCTGGCTGGCTTAGCTGTGCAAGCTGACTTCGGAGATTATAACCAGTT  
 TGATTCCCAAGAGTTCCTCCGAGAGTATGTGCTCTTTCCTATGGATTTGGCCATGGAGGA  
 GCGGCTCTGGAGGAGCTAACCCAGAAGGTGGCCCAGGAACACAAAGCTCATAGCGGGAT  
 CCTGCCGGCTGAAGCTGAAGTGAATGATGTACATCAACGAGGTAGAGCGTTTGGATGGATTTGG  
 ACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGGCATCTTCTT  
 CATGGGGATTTTTTGTGAGGAACAGGGTTCGGGAGACAGGCAGTGATATACAGGTGGAATGA  
 CATTGGGAGTGTACTCACAGCAAAGCAGCCATCCTGTTGGAGCTGATTGACAAGGAGGA  
 GACCGCTCTTCCATACAGATGATATTGAAAATGCCAAGTACATTTCTCGGTTGTTTAC  
 CACTCGGCACAAATTTTACAAACAGAACAAAGATCTGCACTGAACAGTCAAATTTCTCCACC  
 CCAATCAGACGCCAGCCACCTGGAGCCGGTCTCACTGCCAAGGCAGCAGCCGTATAT  
 CTTGCCCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCATACTTCCCAAGA  
 CAGCATTTTCCCCGGGAACGAAGAAGCCTTGTACTGCCGTTCTCACAACAGCCTGGACCT  
 TAATTACTTGAACGGCACCGTCAACCAATGGCAGCGTGTGCAGCGTTCACAGCGTCAACTC  
 CCTCAGCTGCTCCAGAGCTTCATTACAGGCGTCTCCAGTGTCTCCAACCTTAGCATCCC  
 TGGGAGTGACATCATGAGGGCCGATTACATCCCCAGCCACCGCCACAGCACCATCATCGT  
 GCCGTCTTACAGGCCGACCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCT  
 GATGCACGCAGACAGCCAGAGCCGGTCTCTGCGTAACCTCAATATCATCAACACCCATGC  
 CTATAACCAGCCCCGAGGAACCTGGTGTACAGCCAGCCGGAGATGCGGGAGAGGCATCCCTA  
 CACGGTCCCCTATGCACACCAGGGGTGCTACGGTCACAAACTTGTAAGTCCGTCTGACCA  
 GATGAACCCCCAAAATTGTGCGATGCCATCAAGCCAGGGGCCAGTTCCATCTCTCACAC  
 AGTGAGCACTCCAGAACTAGCCAACATGCAGCTCCAAGGAGCACAACTATAGCACAGC  
 CCACATGCTCAAGAACTATCTATTACAGGCCGCCACCCCTTACCCTCGGCCCCGTCTCTGC  
 CACCAGCACCCAGACCTCGCCAGCCACCGCCACAAGTACGTCAGCGGCAGCAGCCCTGA  
 TCTGGTAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACCTGT  
 GGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCCTCACAGCCACCAAGCACCATGGCGG  
 CGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTGATGAACAGCATGGTGAGAGG  
 CATGGAGGCCATGACACTGAAGTCACTCAATATCCCCATGGCTCGCCGCAACACCCTTCG  
 GGAGCAGGGCCCTTCCGAGGAGACGGGCGGCCACGAAGTGCACGGTCTCCCCCAGTATCA  
 CCACAAGAAGACATTCTCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGA

FIGURE 2A

GGAGGAGACCCTGGAGGCTGCACCTCAGGTTCCCTGTGCTTCGAGAGAAAGTAGAATACAG  
 TGCCCAGCTGCAGGCTGCCCTGGCCCGCATCCCCAACAGGCCCCCACCTGAGTACCCAGG  
 GCCAAGAAAAAGTGTCTAGTAATGGGGCACTGAGACAGGACCAGGGAACCCCTCTTCCTGC  
 CATGGCCAGGTGCAGGGTGTCTGAGACACGGACCATCCAAGGCCCTCAGTGTCTCCCGGGC  
 AGAGCAGCTGGCTGTCAACGGTGCCTCTCTGGGTCCCTCCATCTCTGAGCCTGACCTAAC  
 CAGCGTGAAGGAGCGGGTCAAGAAAGAGCCTGTGAAGAAAGGCCGGTGTCTCAGAGATGTT  
 CTCCTGGAGGACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAA  
 GATGACGGGCCCCGAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAATGGGCTCTC  
 GGTGGCCCCGAGTGTCTGGGGCGGGAAGATGGTCTGCCATGATGCCACCCGAGTCCCCATAGA  
 CGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAGATGGAATGGTGTTCACAGAATATGA  
 GCAGATTCCAAACAAAAAGGCCAACGGCGTCTTCAGCACCGCCACTCTGCCTGAGAACGC  
 CGAGCGCAGCCGGATCCGAGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCC  
 GACCAAAGAAAAACAACACAGGCTATATCAACGCCTCCACATCAAGGTGGTGGTCTGGCGG  
 ATCAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGACTTCTG  
 GCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACTGCAGAGGAGGAGGG  
 TGGACGGACCAAAGCCATCGATACTGGCCCAAAGTGGGGTCCAAGCATAGTTCTGCCAC  
 CTACGGCAAGTTCAAGGTCACCACAAAGTTCCGGACAGATTCTGGTTGCTATGCAACGAC  
 GGGCCTAAAGGTGAAGCACCTGCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGCAGTA  
 CACGGACTGGCCCCACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTGTCTACTTGGA  
 GGAAATCCAGTCAGTCCGACGCCACACCAACAGCGTGTCTGGAAGGCATCAGGACCAGGCA  
 CCCCCCATCGTGGTTCACTGCAGCGCGGGTGTGGGAAGGACTGGTGTGGTTATCCTCTC  
 TGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGGAGGTGCCACGATGCTGCG  
 ATTCCTCAGGGAGCAGAGGATGTTTCATGATCCAGACCATTCGCGCAGTACAAGTTCGTCTA  
 CCAAGTCTCGTCCAGTTCCTGCAGAAATCCAGGCTCATTTGATCTCCTCCGGGATGCAG  
 CTTCTGGAGGAGGGACGCAGCTCTGTCCTGCAGGGGGCGGCCACTTCGACAACATCTGCC  
 TCCCCCAGCCAGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATC  
 ATGTATTATTTTATATAAGATAATTTATTTTTTTCCCTCTTTGGAATAAGTTCTGTGAGT  
 TATTATATAATGCTTCCCCCCCCATACACACACAATAATATAGTGCTTCTCATTTG

FIGURE 2B

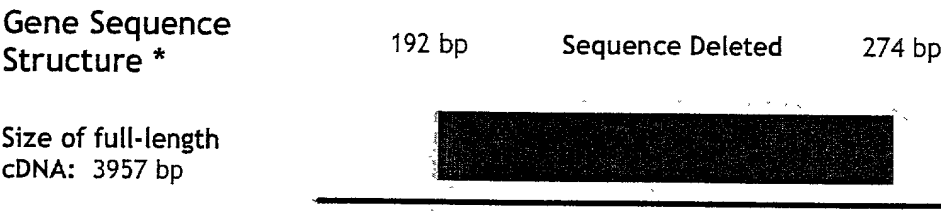


FIGURE 3

Targeting Vector\*  
(genomic sequence)

Arm Length:  
5': 3.5 kb  
3': 2 kb

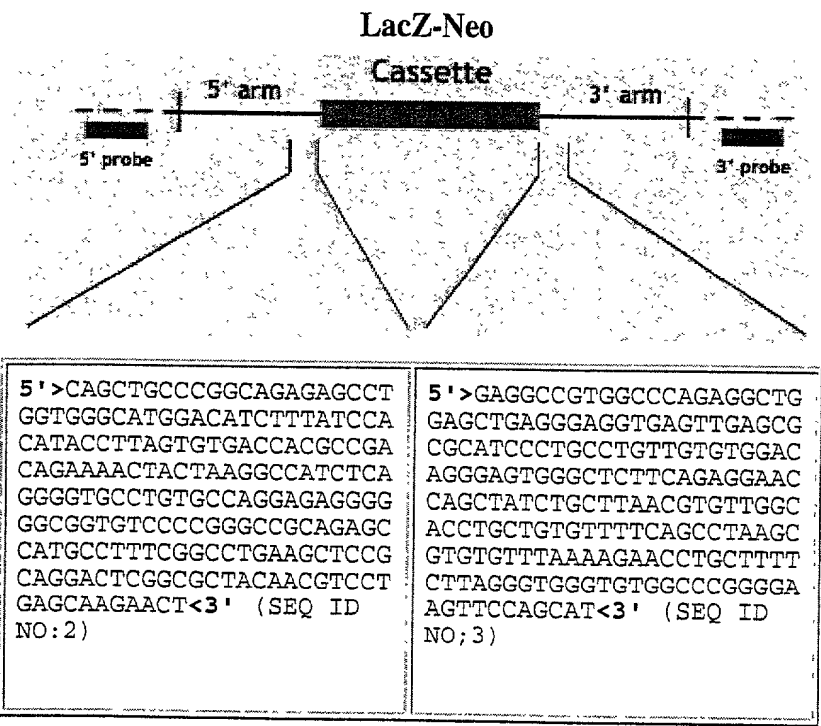


FIGURE 4